CLAIMS

1. A method for manipulating or formulating a solid substance which melts under pressure of a gas without degrading at a temperature which is lower than the melting point of the substance at atmospheric pressure including:

applying to the substance a liquefied gas or dense gas to melt the substance without degrading the substance;

then contacting the molten substance with a carrier fluid, which is at substantially the same pressure as the liquefied gas or dense gas, to form a solution or mixture of at least a part of the molten substance and the carrier fluid; and

passing the solution or mixture into a vessel of lower pressure than the pressure of the liquefied gas or dense gas and carrier fluid to form particles of the substance.

2. A method according to claim 1, wherein the contacting step is conducted at relatively constant temperature and pressure.

3. A method according to claim 1 or claim 2, wherein the carrier fluid is the same as the liquefied gas or dense gas.

4. A method according to any one of claims 1 to 3 further including allowing the substance and the liquefied gas or dense gas to equilibrate for at least one minute before the contacting step.

5. A method according to claim 4, wherein the equilibration step is for a period of about 2 hours.

6. A method according to any one of claims 1 to 5, wherein the substance is a pharmaceutical or biological compound.

7. A method according to claim 6 wherein the substance is cyclosporine.

8. A method according to any one of claims 1 to 7, wherein the temperature is between 5°C and 150°C.

9. A method according to any one of claims 1 to 8, wherein the pressure of the liquefied gas or dense gas and carrier gas is between 5 bar and 200 bar.

10. A method according to any one of claims 1 to 9 wherein the liquefied gas or dense gas is carbon dioxide.

11. A method according to any one of claims 1 to 10, wherein the solution is sprayed through a nozzle.

12. A method according to any one of claims 1 to 11, wherein at least 50% of the particles formed are between 50 and 5000 nanometers in diameter.

13. A method according to any one of claims 1 to 12, wherein over 50% of the particles are less than 5000 nanometers in diameter.

14. A method according to any one of claims 1 to 13, wherein the particles are encapsulated, the method further including the addition of an encapsulating material.

15. A method according to claim 14, wherein the encapsulating material is polymeric after the passing of the solution or mixture.

16. A method according to claim 15 wherein the encapsulating material is biodegradable.

17. A method according to any one of claims 14 to 16, wherein the encapsulating material is selected from the group consisting of polyethylene glycol, polyvinylpyrrolidone, poly(d,*l*-lactide-*co*-glycolide), poly cellulose acetate.

18 A method according to any one of claims 14 to 17, wherein the encapsulated particles contain a mixture or combination of the substance and the polymer for sustained release applications.

19 A method according to any one of claims 14 to 18, wherein more than one pharmaceutical or biological compound is precipitated to form micronised particles.

20. Particles of a substance formed by a method according to any one of the previous claims.

21. Encapsulated particles of a substance formed by a method according to any one of claims 14 to 19.

22. Particles according to claim 20 or claim 21, wherein the particles include a pharmaceutical or biological substance.

23. Particles according to claim 22 wherein the particles include primarily cyclosporine.

24. Particles according to any one of claims 20 to 23, wherein at least 50% of the particles are between 50 and 5000 nanometers in diameter.

25. Particles according to claim 24, wherein all the particles are less than 5000 nanometers in diameter.

26. A composition suitable for aerosol delivery including particles formed by a method according to any one of claims 1 to 19.

27 A method of treatment of a subject including administering to the subject an effective amount of fine particles of a substance produced by a method according to any one of claims 1 to 19.

28. A method according to claim 27 wherein the substance is a pharmaceutical or biological compound.

29. A method according to claim 27 or claim 28 wherein the administration of the substance is by inhalation.

30. A method according to claim 27 or claim 28 wherein the administration is by transdermal application, oral, controlled or sustained release.

31. An apparatus for producing particles by the method according to any one of claims 1 to 19, including:

a pressure chamber having an inlet and an outlet, the outlet being above the inlet;

a first conduit means connected to the inlet for supplying the liquefied gas or dense gas to the pressure chamber; and

a second conduit means extending from the outlet to a depressurisation point.

32. An apparatus according to claim 31, further including flow control means to control flow along the second conduit means.

33. An apparatus according to claim 32, further including a third conduit means connected to the downstream end of the second conduit means downstream of the flow control means for supplying liquefied gas or dense gas, or carrier fluid, at pressure to the depressurisation point.

34. An apparatus according to any one of claims 31 to 33, wherein the depressurisation point is a nozzle.

35. An apparatus according to any one of claims 31 to 34, wherein the apparatus upstream of the depressurisation point is maintained at a constant temperature by a temperature bath.

36. A pharmaceutical composition including particles of a substance produced by a method according to any one of claims 1 to 19.

37. A pharmaceutical composition according to claim 36, wherein the substance is a pharmaceutical or biological compound.

38. A pharmaceutical composition according to claim 37, wherein the substance is cyclosporine.

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